REMARKS

The claims are not obvious under 35 USC §103

Claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31 and 33-46 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the Bankneider *et al.* US Patent 4,751,243 reference, in light of the York US Patent 4,600,717 reference and the DiPiro *et al.* publication. FDA Guideline No. 38 and Chen *et al.* US Patent 6,232,341 are referenced to show the state of the art as to methods of assessing the efficacy of topical therapeutic preparation in treating skin wounds. Applicants respectfully traverse.

Initially, Applicants respectfully contend that the Action continues to assert that the claims will be construed for examination to encompass ophthalmic wounds. Applicants respectfully submit that they have limited their claims to wounds to the dermis or epidermis, terms the skilled worker would understand do not encompass ophthalmic injuries. Applicants have made this point repeatedly during prosecution, and request that the Office recognize this distinction. Should the Examiner require that this limitation be explicitly recited in the claims, Applicants ask her indulgence to suggest a manner of making the limitation that would be acceptable. Since in their view the claims are already limited to wounds that are not ophthalmic in location, the Office will understand Applicants' reticence to guess on this point.

Moreover, the assertion of the DiPiro reference in response to Applicants' earlier arguments is inapposite. Applicants did not argue that it was not within the skill of the art to make a topical formulation (the only teaching in the DiPiro reference), but rather than their method of identifying an aldose reductase inhibitor for topical administration to facilitate wound healing in a diabetic animal was not obvious in light of systemic use of ARIs. Applicants thus respectfully request that the Office respond to the argument Applicants are making rather than to ones they have not.

Applicants respectfully contend that the cited art, taken alone or in combination would not have provided any basis for the skilled artisan to have combined these references or to achieve the claimed invention. There is no common technical problem addressed by these references, nor do the references provide a solution to any problem known in the art addressed by the present invention. Specifically, the skilled artisan would not have been motivated to consider the cited art directed to aldose reductase inhibitor compounds (ARIs) known and used for systemic administration

for treating wounds or ophthalmic injuries for treating wounds topically; specifically, this art would not have motivated the skilled worker to treat skin wounds created by punch biopsy to be measured by rate intervals of wound healing.

> *According to the MPEP, Section 2142, paragraph 3, "To establish a prima facie case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references to combine reference teachings. Second, there must be reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations. The teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure."*

Turning to the Action, it is acknowledged by the Patent Office that the Bankneider reference teaches administration of the aldose reductase inhibitor tolrestat systemically and fails to disclose topical administration thereof. The reference is also devoid of any teaching related to punch biopsy to produce a wound. The Action also concedes that the York reference is limited to administration to the eye, and that this differs from the topical administration taught by the present invention. Furthermore, the Patent Office has agreed that the ocular tissue differs from dermal/epidermal tissue. Also, the Chen reference is particularly limited to reepithelialization and prevention of scarring resulting from burns and methods for testing agents (not aldose reductase inhibitors) using experimentally-induced burns (which are recognized in the art as being different from the types of wounds produced using the punch biopsy method disclosed in the instant application). Moreover, the Chen reference is not concerned with neuropathy of the underlying tissue as disclosed in Applicant's specification.

Finally, DiPiro is directed solely to show that the art contained teachings regarding how to make a topical or ophthalmic formulation of an active pharmaceutical ingredient. Applicants note that the pending claim set does not contain any claims relating to the subject matter of the DiPiro reference.

Applicants respectfully contend that, at best, the Action provides support for the proposition that the invention may have been obvious to try. However, "obvious to try" has never, by itself, been sufficient to make out a prima facie case of obviousness. For example although obvious to try an invention cannot be obvious when the art gives "no indication *which* parameters were critical or *no*

direction as to which of many possible choices is likely to be successful" or gives "*only general guidance* as to the particular form of the claimed invention or how to achieve it." *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). This standard has not been changed by the Supreme Court's recent *KSR v. Teleflex* decision, where the Court said:

> . . . When there is a design need or market pressure to solve a problem and there are a *finite number* of *identified, predictable* solutions, a person of ordinary skill has good reason to pursue the *known options* within his or her technical grasp. If this leads to the *anticipated success*, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103. (*emphasis added*)

KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1731 (2007).

Here, there is no finite number of identified, predictable solutions for treating wound healing or other neuropathies is a diabetic patient, nor would the practice of the claimed invention lead to an anticipated successful result. The Chen reference, cited in support of the asserted obviousness rejection, in fact teaches that what can be expected in instances of topical administration of drugs or drug lead compounds include that they are found to "both irritating and toxic" and "may result in contact dermatitis" or "are found to make some complications (such as fungal infections) worse." Chen, pg. 1, Background of the Invention. These teachings include a wide variety of compounds to be tested for topical administration, including anti-bacterial agents, antibiotics, and compound preparations with corticosteroids - all of which have diverse chemical formulae and properties. Thus, the art teaches that topical administration is in fact *unpredictable*.

Applicants respectfully contend that none of the cited art is directed to the claimed invention, and that the art that is relevant thereto - Chen - actually teaches that the subject matter of the invention is unpredictable. In view of these characteristics of both the art and the invention, Applicants respectfully submit that legal precedent requires the conclusion that even if the claimed invention may have been obvious to try, it is not obvious. Applicants thus respectfully request that the Examiner withdraw these grounds of rejection and pass the pending claims to allowance.

CONCLUSION

It is believed that all requirements of patentability are fully met, and allowance of the claims is respectfully requested. If the Examiner believes it to be helpful, the Examiner is invited to contact the undersigned attorney by telephone at 312-913-0001.

Respectfully submitted,
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